

World Journal of *Clinical Cases*

World J Clin Cases 2022 April 6; 10(10): 2976-3320



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INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJCC* as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The *WJCC*'s CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Xu Guo*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lai Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

April 6, 2022

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/gerinfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/gerinfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/gerinfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Dedifferentiated chondrosarcoma of the middle finger arising from a solitary enchondroma: A case report

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Specialty type: Orthopedics

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Yang L, Yao W

Received: November 15, 2021

Peer-review started: November 15, 2021

First decision: January 11, 2022

Revised: January 19, 2022

Accepted: February 20, 2022

Article in press: February 20, 2022

Published online: April 6, 2022



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Abstract

BACKGROUND

Dedifferentiated chondrosarcoma (DDCS) accounts for 10% of all chondrosarcomas and has the poorest outcome, with a 5-year survival rate of 7%-25%. DDCS commonly occurs in the femur and pelvis, whereas DDCS of the finger is extremely rare. Furthermore, the histological findings of preexisting solitary enchondroma samples are important and valuable for diagnosing malignant transformations.

CASE SUMMARY

We report our experience with DDCS in the proximal phalanx of the left middle finger of an 87-year-old woman. She had undergone surgery for enchondroma, with curettage and artificial bone grafting, 11 years ago, in the same location. Several years after the primary surgery, the left middle finger gradually started to enlarge, and the growth speed increased in the past year. Plain radiographs showed an expansive osteolytic lesion with calcifications and residual grafting material. Owing to the suspicion of malignancy, we performed ray amputation. Histological findings revealed an abrupt transition between the low-grade chondrosarcoma and dedifferentiated sarcoma components. The dedifferentiated components showed the features of a high-grade undifferentiated pleomorphic sarcoma. The patient was diagnosed with DDCS arising from a preexisting enchondroma. She had no local recurrence or distant metastasis and died of

pneumonia 6 years and 10 months after the second surgery.

CONCLUSION

The histological findings of a precursor lesion showed a typical enchondroma, suggesting that DDCS can arise from enchondroma.

Key Words: Dedifferentiated chondrosarcoma; Enchondroma; Finger; Phalanx; Ray amputation; Case report

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Core Tip: Dedifferentiated chondrosarcoma (DDCS) is a very rare primary malignant bone tumor. Furthermore, malignant transformation of a single enchondroma of the hand bone into DDCS is considered extremely rare, with no detail of precursor pathological findings being reported previously. There have been no reports showing preexisting enchondromas prior to wide resection. Our report evaluated the histological findings of a precursor lesion, and the specimen showed a typical benign enchondroma, suggesting that DDCS can arise from enchondroma.

Citation: Yonezawa H, Yamamoto N, Hayashi K, Takeuchi A, Miwa S, Igarashi K, Morinaga S, Asano Y, Saito S, Tome Y, Ikeda H, Nojima T, Tsuchiya H. Dedifferentiated chondrosarcoma of the middle finger arising from a solitary enchondroma: A case report. *World J Clin Cases* 2022; 10(10): 3297-3305

URL: <https://www.wjgnet.com/2307-8960/full/v10/i10/3297.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i10.3297>

INTRODUCTION

Primary chondrosarcoma is the third most common primary malignant tumor of the bone[1]. The most commonly involved sites are the femur and pelvis. In contrast, the small bones of the hands and feet, which mainly harbor enchondromas, are rarely involved in primary chondrosarcoma[2,3]. Dedifferentiated chondrosarcoma (DDCS), which was introduced by Dahlin and Beabout[4], refers to a high-grade sarcoma occurring next to a low-grade malignant cartilage-forming tumor, which generally resembles an enchondroma or low-grade conventional chondrosarcoma. The dedifferentiated portion of the lesion may comprise a wide variety of mesenchymal neoplasms, such as undifferentiated pleomorphic sarcomas, osteosarcomas, fibrosarcomas and rarely rhabdomyosarcomas[4,5]. Typically, histologic findings have a sharp demarcation between the low-grade cartilaginous and high-grade components[4]. It has the poorest outcome, with a 5-year survival rate reported between 7% and 25%[6-9]. Due to the rarity of the diagnosis, only a few extensive studies report the demographic data. In one of these large series, Grimer *et al*[6] reported that 233 (69.1%) out of 337 tumors involved long bones of the peripheral skeleton whilst 104 (30.9%) involved the axial skeleton (pelvis, rib, *etc.*).

DDCS arising in the small tubular bones of the hands is extremely rare. Furthermore, the histological findings of preexisting solitary enchondroma samples are important and valuable for diagnosing malignant transformations. Herein, we present a rare case of DDCS developing in the proximal phalanx of the left middle finger. In addition, this report shows a histological specimen of the preexisting enchondroma. To our knowledge, this is the first case report of the DDCS of the finger, with detailed histological findings of both enchondroma and DDCS.

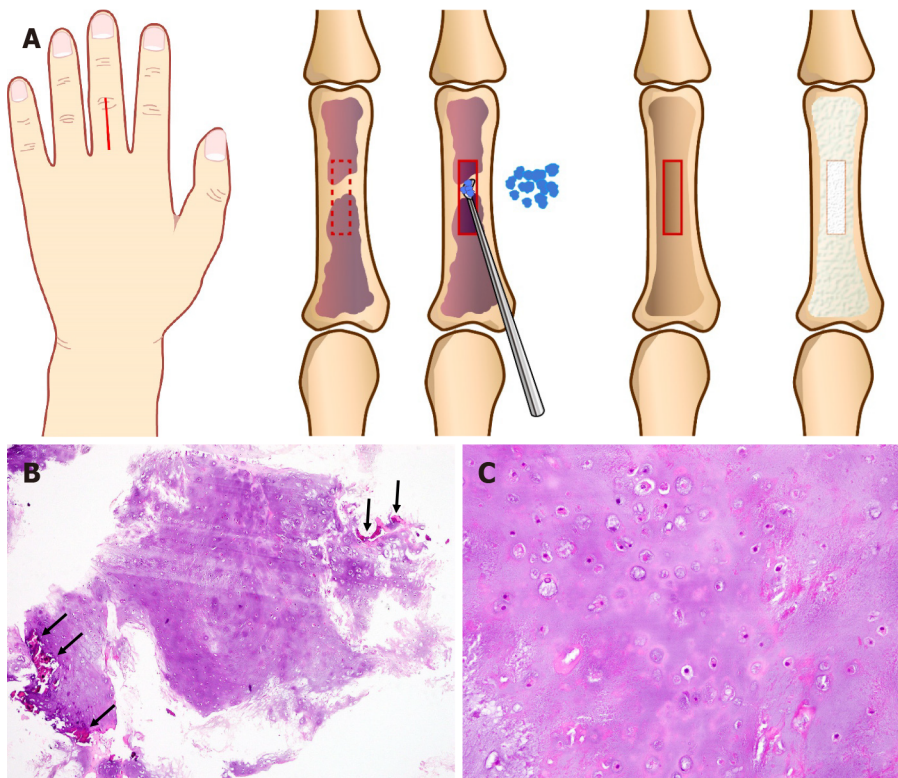
CASE PRESENTATION

Chief complaints

An 87-year-old woman presented with pain and enlarged mass of left middle finger.

History of present illness

At 76 year old, the patient complained of finger pain due to a mallet finger. The radiographs incidentally revealed a typical enchondroma of the proximal phalanx of the left middle finger. To prevent pathological fracture, curettage was performed under axillary nerve block. The cortex adjacent to the lesion was approached dorsally, splitting the extensor tendon. After fenestration of the bone cortex, curettage and packing of the granular artificial bone graft made of hydroxyapatite were performed (Figure 1A). The histological examination revealed a hypocellular area, with an abundance of hyaline cartilage matrix, and the lesion was diagnosed as an enchondroma (Figure 1B and C). Several



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Figure 1 Schema and histological findings of the primary surgery at 76 years of age. A: Schema of the primary surgery referencing the surgical record and figures. The tumor is located in the third proximal phalanx. After fenestration of the bone cortex, curettage and granular artificial bone grafting were performed under axillary nerve block. B: Magnification $\times 4$. The tumor appears as a lobular, relatively cell-poor hyaline cartilage surrounded by an eosinophilic zone of reactive bone formation (encasement pattern; arrow). C: Magnification $\times 20$. Scattered chondrocytes are located in sharp-edged lacunar spaces, with abundant hyaline cartilage matrix. Nuclei are small, round, and hyperchromatic, although larger, vesicular nuclei can also be present. No nuclear pleomorphism or enlargement is observed.

years postoperatively, the left middle finger gradually started to enlarge, and the growth speed increased in the past year.

History of past illness

She underwent an excision of uterine leiomyoma 30 years previously.

Personal and family history

She had no significant personal or family history.

Physical examination

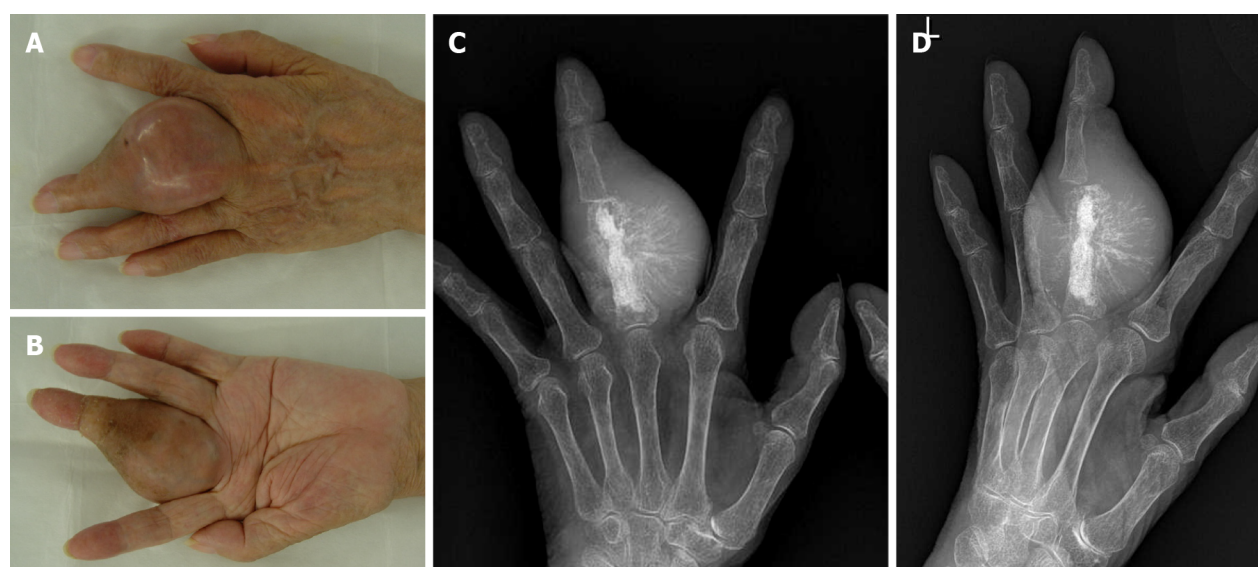
Her physical findings at our clinic were as follows: Height, 145 cm; weight, 42 kg; and body mass index, 20.0 kg/m². The left middle finger appeared swollen and tense (Figure 2A and B). The size of the tumor was 5.5 cm $\times$ 5.5 cm $\times$ 4.5 cm, and it was elastic and hard.

Laboratory examinations

Her laboratory test results were as follows: hemoglobin, 12.1 g/dL (normal range, 11.2-14.5); total leukocyte count, 6040/ μ L (normal range, 3300-8800); platelet count, 240000/ μ L (normal range, 130000-350000); erythrocyte sedimentation rate, 49.0 mm/hour (normal range, 0.0-15.0); C-reactive protein, 0.1 mg/dL (normal range, 0.0-0.14); lactate dehydrogenase, 152 IU/L (normal range, 119-229); and alkaline phosphatase (Japan Society of Clinical Chemistry; JSCC), 207 IU/L (normal range, 115-359).

Imaging examinations

Plain radiographs showed residual artificial bone graft material and an expansive osteolytic lesion in the proximal phalanx of the left middle finger (Figure 2C and D).



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Figure 2 Clinical photographs and X-ray of the finger 11 years after the primary surgery. A and B: Clinical photographs of the hand at 87 years of age. The left middle finger appears swollen and tense. The scar of the primary surgery is observed in the dorsal surface of the middle finger; A: Dorsal view; B: Palmar view; C and D: The X-ray shows residual artificial bone graft material and an expansive osteolytic lesion in the proximal phalanx of the middle finger; C: Anteroposterior view; D: Oblique view.

FURTHER DIAGNOSTIC WORK-UP

Chest computed tomography showed no lung metastases.

PREOPERATIVE DIAGNOSIS

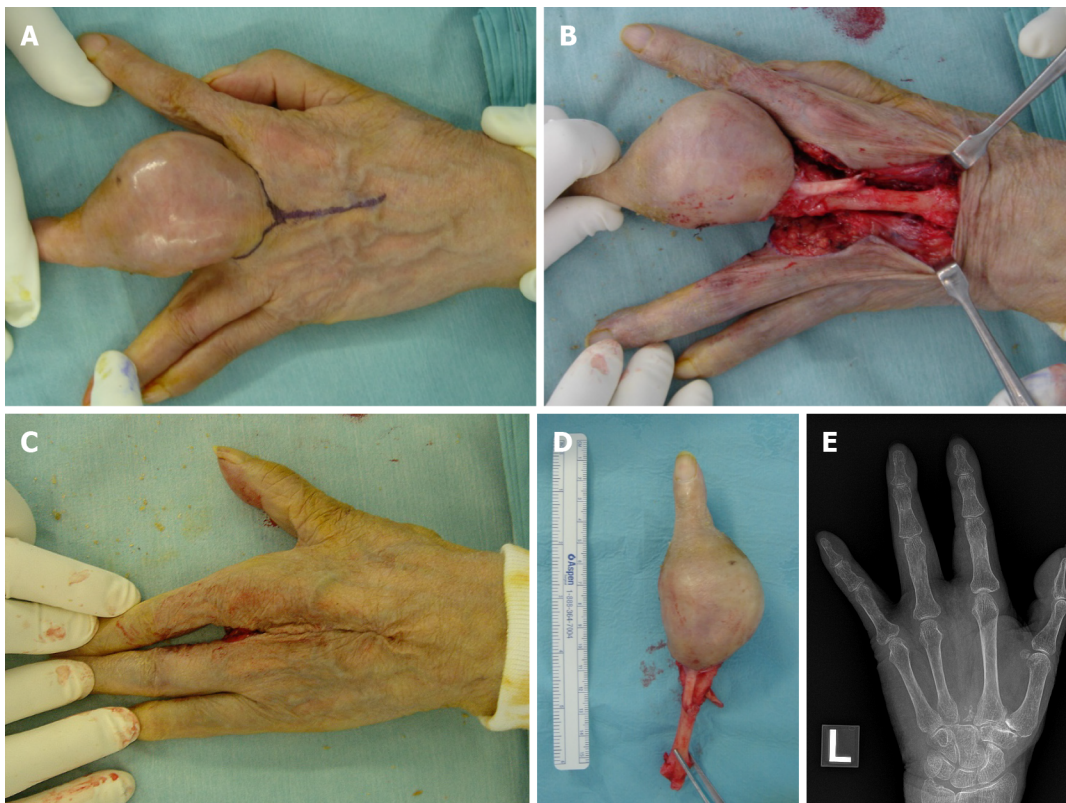
The diagnosis prior to operation was chondrosarcoma of middle finger arising from a preexisting enchondroma.

FINAL DIAGNOSIS

DDCS of middle finger arising from a preexisting enchondroma.

TREATMENT

Conventional chondrosarcoma developing from a preexisting enchondroma was suspected, and ray amputation was performed, which involved excision of the entire middle metacarpal and careful soft tissue repair (Figure 3A-E). Removal of the metacarpal base created a good four-finger hand from both a functional and cosmetic viewpoint. The gross examination of the amputation specimen revealed a 4.5 cm × 4.3 cm × 5.5 cm tumor located mainly in the proximal phalanx and the tumor extended to the soft tissue below the skin. The cut surface of the intraosseous tumor had a chondroid-looking matrix with central calcified areas, consistent with the plain radiographic findings, while the other component was fleshy and tan-white (Figure 4A). The microscopic examination revealed that the tumor consisted of two morphologically distinct parts. A considerable part of the tumor showed chondroid areas with low-grade chondrosarcomatous morphology, and a small part of it had fibrous tumor cells showing nuclear pleomorphism, hyperchromatism and abnormal mitoses, consistent with those of high-grade undifferentiated pleomorphic sarcomas (Figure 4B). The cartilaginous portion of the tumor showed grade 1 or grade 2 chondrosarcoma with bone destruction. We also observed a residual hydroxyapatite artificial bone graft used 11 years ago (Figure 4C). The high-grade dedifferentiated area was composed of spindle cells arranged in a fascicular growth pattern. Cellularity was prominent and the tumor showed necrosis; however, no osteoid or bone matrix production was noted (Figure 4D). Immunohistochemically, the dedifferentiated portion was negative for the α -smooth muscle actin, desmin, CD34, S-100 protein, and epithelial membrane antigen. This high-grade dedifferentiated component accounted for 10.2% of the tumor in the maximum cross-section (Figure 4A). The surgical margins were negative. Postoperative



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Figure 3 Intraoperative photographs and postoperative X-ray of the second surgery at 87 years of age. A: A racket-shaped incision was planned; B: The third metacarpal bone is exposed and disarticulated at the carpometacarpal joint; C: The postoperative photograph of the dorsal aspect of the left hand demonstrates the gap closure; D: The amputated specimen; E: The postoperative X-ray of the left hand shows a good cosmetic four-finger hand.

pathology results and immunohistochemical results indicated DDCS of the middle finger arising from a preexisting enchondroma.

OUTCOME AND FOLLOW-UP

There was no local recurrence or distant metastasis. She did not undergo any additional chemotherapy or radiotherapy and died of pneumonia 6 years and 10 mo after the ray amputation (Figure 5).

DISCUSSION

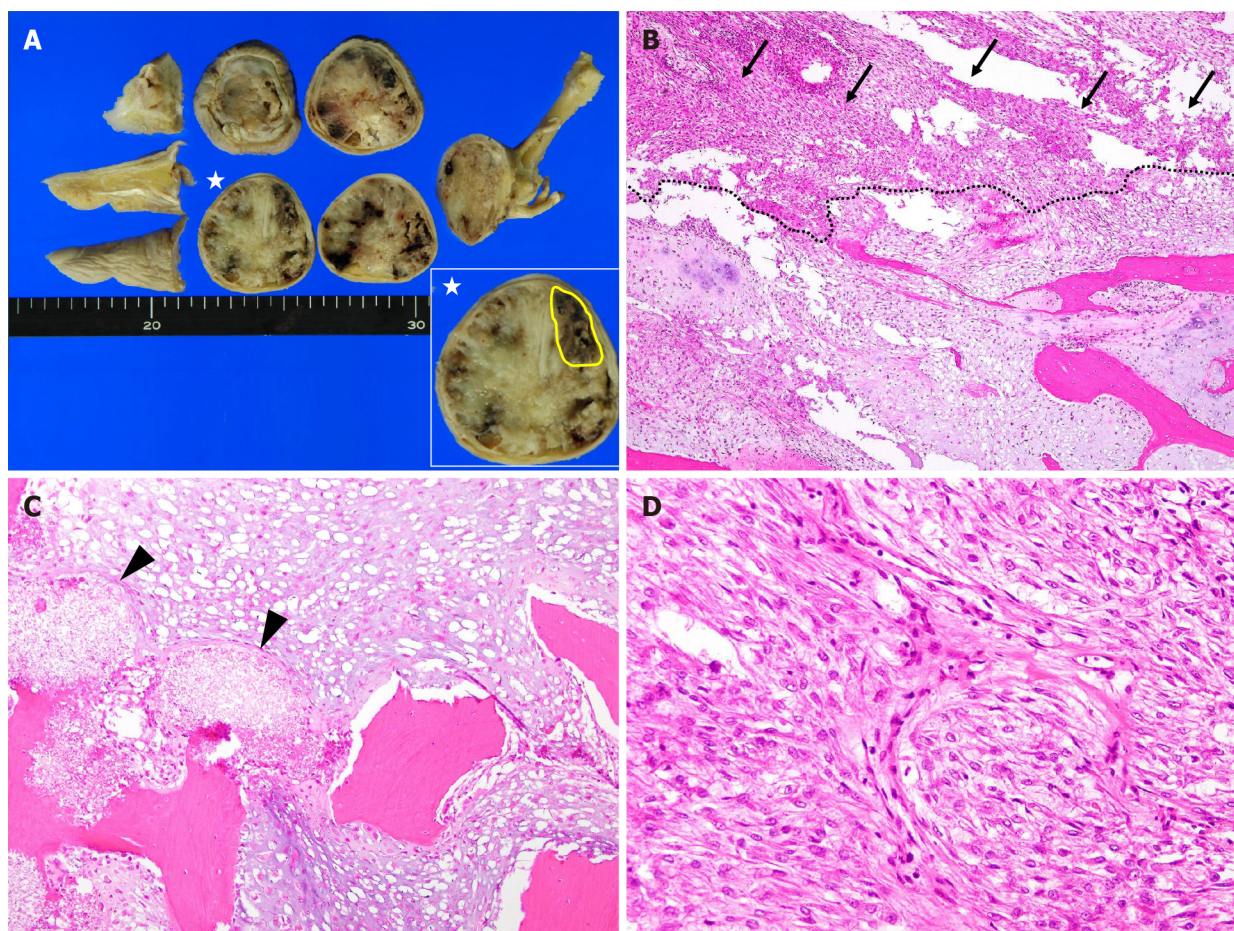
DDCS is defined as a nonchondrogenic, high-grade sarcoma associated with a well-differentiated chondrosarcoma, with an abrupt transition[4]. Grimer *et al*[6] reported that the median age of these cases was 59 years (range: 15-89 years), and there was a slight predominance of men[6]. The average size of the tumor at diagnosis was 12.6 cm[6].

The most common location of DDCS is in the femur[6,10]. Grimer *et al*[6] reported that the tumor involved the femur in 154 patients (45.7%), pelvis in 95 (28.2%), humerus in 37 (11.0%), scapula in 18 (5.3%), and other locations in 33 (9.8%). In total, 233 tumors involved the long bones of the peripheral skeleton, while 104 involved the axial skeleton (pelvis, rib, *etc.*)[6]. Johnson *et al*[10] reported that the tumors were located in the femur in eight cases (30.8%), ilium in four (15.4%), humerus in three (11.6%), ischium in two (7.7%), acetabulum in two (7.7%), pubic ramus in two (7.7%), rib in two (7.7%), scapula in one (3.8%), fibula in one (3.8%), and tibia in one (3.8%). DDCS of the finger is extremely rare with only two case reports being available till date (Table 1). Doganavsargil *et al*[11] reported a case of DDCS developing in the proximal phalanx of the left thumb of a 66-year-old man. The high-grade component showed fibrosarcoma-like findings. The patient was treated with amputation and died of the disease within 9 months after the surgery. Liu *et al*[12] reported a case of DDCS of the right finger in a 32-year-old man. The high-grade component of this case was spindle cell sarcoma, and the patient was treated with amputation and alive 18 mo after the surgery[12]. In our case, radical amputation was performed with an adequate surgical margin, and there was no local recurrence or distant metastasis for over 6

Table 1 Summary of the characteristics of three cases of dedifferentiated chondrosarcoma of the finger in the literature

Author, yr	Sex	Age	Location	Symptoms	Treatment	Recurrence	Lung metastasis	Oncological outcome	Follow-up
Doganavsargil <i>et al</i> [11] 2009	M	66	L thumb	Pain, swelling	Amputation	No	Yes	DOD	9 mo
Liu <i>et al</i> [12] 2017	M	32	R finger	Pathological fracture	Amputation	No	No	AWD	18 mo
Present case	F	87	L middle finger	Pain, swelling	Amputation	No	No	DOC	6 yr 10 mo

M: Male; F: Female; R: Right; L: Left; DOD: Died of disease; AWD: Alive with disease; DOC: Died of other causes.



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Figure 4 Histological findings of the amputated specimen. A: Macroscopically, the tumor has destroyed the bone cortex and is extended to the soft tissue below the skin. The tumor is a grayish-white hyaline cartilage component filling the medullary cavity with hemorrhage and necrosis. In the largest cross-section of the tumor (star), the high-grade dedifferentiated component (yellow) accounts for 10.2% of the tumor; B: Magnification $\times 4$. There is an abrupt transition between the low-grade chondrosarcoma (lower side) and high-grade dedifferentiated sarcoma components (upper side; arrow); C: Magnification $\times 10$. The cartilaginous portion of the tumor shows a grade 1 or grade 2 chondrosarcoma with bone destruction. Arrowheads show the hydroxyapatite artificial bone graft that was used 11 years ago; D: Magnification $\times 20$. The high-grade dedifferentiated component shows mitoses and atypia. The lesion is composed of spindle cells arranged in a fascicular growth pattern, resembling a high-grade undifferentiated pleomorphic sarcoma.

years postoperatively.

Malignant transformation of a single enchondroma of the hand bone into a chondrosarcoma is considered extremely rare and unusual[2,3]. Müller *et al*[2] reported a case of malignant transformation of a benign enchondroma of the hand into a secondary chondrosarcoma. Culver *et al*[3] reported a chondrosarcoma of the hand arising from a preexisting solitary enchondroma. However, they only evaluated the amputated specimen and histological findings showed a secondary chondrosarcoma and enchondroma in the same specimen. No reports have shown preexisting enchondromas prior to wide resection. Our report evaluated the histological findings of a precursor lesion, and the specimen showed



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Figure 5 Computed tomogram of the 94-year-old woman, 6 years and 9 months after the second surgery. The axial chest computed tomogram shows bilateral pleural effusion due to chronic congestive heart failure. No lung metastases are observed.

a typical benign enchondroma, suggesting that DDCS can arise from an enchondroma. Some authors have reported a specific mutation that can promote the development of DDCS. Grote *et al*[13] reported evidence that the p53 mutation may be regarded as at least a co-factor that “switched” the preexisting low-grade conventional chondrosarcoma into a highly malignant dedifferentiated tumor. The expression of membrane-type 1 matrix metalloproteinase also plays an important role in the morphological degradation of the cartilaginous matrix with an increasing histological grade[14]. Franchi *et al*[15] suggested that alterations of genes implicated in regulating the G1-S phase cell cycle checkpoint contribute to the process of dedifferentiation in peripheral secondary chondrosarcoma. Yang *et al*[16] reported that combining clonality analysis with isocitrate dehydrogenase 1 (IDH1) and IDH2 mutation detection revealed that cartilaginous and non-cartilaginous components of DDCS originate from the same primitive cells, which must have the potential to differentiate into cartilage.

An abrupt transition occurs between the conventional hyaline cartilage and high-grade sarcoma components of DDCS[4]. The cartilaginous portion can range from an enchondroma-like appearance to grade 1 or grade 2 chondrosarcoma[17]. The high-grade dedifferentiated component generally has features of mesenchymal neoplasms, such as undifferentiated pleomorphic sarcoma, osteosarcoma, fibrosarcoma and rarely rhabdomyosarcoma[4,5]. In our case, the high-grade component showed undifferentiated pleomorphic sarcoma-like findings.

Patients with DDCS have a dismal prognosis, most often as a result of widespread lung metastases [17]. Overall 5-year survival rates of 7%-25% have been reported[6-9]. DDCS appears to be resistant to the currently available chemotherapy. The best possibility of cure is linked to the excision of the tumor with clear surgical margins[6]. Poor prognostic factors include a tumor size > 8 cm, the presence of a pathological fracture, presence of a metastatic disease at diagnosis, pelvic location, inadequate surgical margin, and non-surgical treatment[6,9,17,18]. In our case, the tumor was resected widely, and the patient had a good prognosis. The patients reported by Sissons *et al*[19] and Levin *et al*[20] also had a good prognosis and survived for 8.5 and 4.5 years respectively, after the initial surgery. This suggests the possibility of a more favorable prognosis for this variant of tumor compared to conventional DDCS [19,21].

CONCLUSION

Our report evaluated the histological findings of a precursor lesion, and the specimen showed a typical enchondroma, suggesting that DDCS can arise from enchondroma.

FOOTNOTES

Author contributions: Tsuchiya H, Tome Y and Yonezawa H served as the patient’s surgeons, reviewed the literature and contributed to manuscript drafting; Ikeda H and Nojima T reviewed the pathological findings and contributed to manuscript drafting; Yamamoto N, Hayashi K, Takeuchi A and Miwa S analyzed and interpreted the imaging findings; Igarashi K, Morinaga S, Asano Y and Saito S were responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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S-Editor: Ma YJ

L-Editor: A

P-Editor: Ma YJ

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